REMARKS

Claims 1-27 are pending in this application. Claims 14 and 21 have been amended. Claims 22-27 have been added. No new matter has been added by way of these amendments and new claims because each amendment and new claim is supported by the present specification. For example, the amendments to claims 14 and 21 merely correct typographical errors, for which support can be found in the specification at page 5, lines 1-6. Support for new claims 22 and 25 can be found in the previous claims and in the specification at page 4, lines 11-16, and at page 5, lines 23-27. Support for new claims 23, 24, 26 and 27 can be found in the original claims and in the specification, for example, at page 3, lines 15-19. Thus, no new matter has been added.

Further, it is noted that many of the amendments made herein are not made for patentability purposes (*e.g.*, to avoid the prior art) which might otherwise raise estoppel issues under the recent holding of *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 56 USPQ2d 1865 (Fed. Cir. 2000). Instead, claims 14 and 21 have been amended to correct the typographical error of a missing comma. Thus, these amendments simply serve to clarify the inventive discovery that the Applicants regard as their own, without narrowing the scope of the same claims.

Based upon the above considerations, entry of the present amendment is respectfully requested.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Issues Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 14 and 21 under 35 U.S.C. § 112, second paragraph, as being indefinite due to the phrase "powders liquids". Applicants respectfully traverse.

Applicants have amended claims 14 and 21 to correct the typographical error by inserting a missing comma. Thus, claims 14 and 21 clearly recite "powders, liquids" as the medicine. Therefore, Applicants respectfully request the Examiner to reconsider and withdraw this rejection.

Issues Under 35 U.S.C. § 103(a)

The Examiner has rejected claims 1-21 under 35 U.S.C. § 103(a) as being unpatentable over Matoba et al. (U.S. Patent 5,464,612; hereinafter Matoba '612) in view of Aoki Shigeru et al. (JP-A 07-267850; hereinafter JP '850) and in further view of Balkin (U.S. Patent 5,656,284; hereinafter Balkin '284). Applicants respectfully traverse this rejection.

The Present Invention and Its Advantages

There are many conventional methods and compositions that prevent an unpleasant taste of a medicine, such as those described in the

specification (for example, see pages 1-2). These conventional methods/compositions include coating a granulated agent with a water-soluble film (as described in JP-A 4-282312), and melting a waxy substance in order to disperse and solidify the medicine (as described in JP '850). These methods do have drawbacks, also described in the specification (page 2, lines 9-14), including compromises of quality and a reduced effectiveness of the medicine itself.

In contrast, the present invention is directed to oral medicine compositions that effectively reduce and prevent the unpleasant taste of basic medicines (*i.e.*, donepezil hydrochloride; (RS)-1-(isopropoxycarbonyloxy)ethyl(+)-(6R,7R)-7-{(z)-2-(2-aminothiazole-4-yl)-2-hydroxyiminoacetamide}-3-N,N-dimethylcarbamoyloxymethyl-8-oxo-5-thia-1-azabicyclo-[4.2.0]octo-2-en-2-carboxylate hydrochloride salt). The present invention is further directed to methods for preventing the unpleasant taste of the basic medicines that include the mentioned oral medicine compositions. Specifically, the claimed oral medicine compositions comprise anionic polymer(s) and the basic medicine, where the anionic polymer is homogeneously mixed with the basic medicine to effectively avoid the unpleasant taste of the medicine.

However, the prior art fails to disclose the claimed combinations and methods comprising the anionic polymers according to the present invention and present claims. This will be discussed in more detail below.

Distinctions over the Combination of Matoba '612, JP '850, and Balkin '284

As mentioned, the present invention is directed to oral medicine compositions, or methods using the same, comprising certain types of polymers, where the claimed compositions prevent the unpleasant taste of basic medicines. However, the references of Matoba '612, JP '850, and Balkin '284, fail in combination to disclose or suggest the claimed orally administered medicine compositions/methods because these references have been improperly combined.

Matoba '612 is generally directed to clad powdery and granular preparations of medically active ingredients and ion exchangers (see Abstract). The disclosed coating composition includes a list of water-soluble polymers, water-insoluble polymers, acid-soluble polymers, and enteric polymers (see Col. 6, lines 18-25). The Examiner asserts that Matoba '612 also teaches basic medications as having a bitter taste, and the amount of the disclosed ion exchanger to be used is about 10 to 50,000 parts by weight per 100 parts by weight of the active ingredient (see Office Action of July 3, 2001, page 3). The Examiner also discusses the disclosures of JP '850 and Balkin '284.

Then the Examiner concludes that one of ordinary skill in the art would be able to substitute the type of polymers of JP '850 and Balkin '284 for the polymers disclosed in Matoba '612 because it serves the same purpose of making medications more palatable (see Office Action, page 4, lines 6-11). However, Applicants respectfully submit that the

USPTO has addressed the wrong analysis for obviousness and nonobviousness under 35 U.S.C. § 103(a).

Applicants submit that it is not possible to combine the above-mentioned references as a basis for rejecting the claimed invention under 35 U.S.C. § 103(a). U.S. case law squarely holds that a proper obviousness inquiry requires consideration of at least two factors: (1) whether or not the prior art would have taught, motivated, or suggested to those of ordinary skill in the art that they should make the claimed invention (or practice the invention in case of a claimed method or process); and (2) whether or not the prior art would have revealed that in making the claimed invention (or practicing the invention in case of a claimed method or process), there would have been a reasonable expectation of success. *See, e.g., In re Vaeck*, 947 F.2d, 488, 493 (Fed. Cir. 1991); *In re Kotzab*, 55 USPQ2d 1313, 1316-17 (Fed. Cir. 2000); *see also In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995) ("Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination."). In other words, the prior art references themselves must state the motivation or suggestion to combine the references.

Therefore, Applicants respectfully submit that the issue regarding obviousness is not whether one of ordinary skill in the art would have been able to substitute Aoki's polymer(s) or Balkin's polymer(s) for

Matoba's polymer, but whether the cited references themselves would have provided such a person having ordinary skill in the art with a motivation to carry out the claimed invention and a reasonable expectation of success in doing so. In the present case, no motivation exists for combining the teachings of the cited references in order to obtain the present invention.

There is no motivation in the cited references for combining these references because Matoba '612 actually teaches away from the present invention. The Examiner states that Matoba '612 teaches mixing a polymer with a basic medicine, and refers to Col. 3, lines 6-10 of the cited reference. However, Applicants respectfully submit that Matoba '612 is directed to an ion exchanger that coats a medicine only, and not mixing the two ingredients. For example, in discussing the term "cladding material", where this material is a feature in the claims of Matoba '612, this cladding material is used to form a barrier between the medicinally active ingredient and the ion exchanger (see Col. 3, 26-35). Even in all of the claims of Matoba '612, the active ingredient is not in direct contact with the medicinally active ingredient, and even directs the reader (*i.e.*, one having ordinary skill in the art) away from concluding that any polymer could be mixed with a medicinally active ingredient (for example, see independent claims 1, 2, 21, 24, and 27). Thus, Matoba '612 fails to disclose, suggest, or make obvious that

an anionic polymer could be homogeneously mixed with a basic medicine to avoid the unpleasant taste.

The Examiner also states that Matoba '612 discloses "several approaches to masking bad taste of medicinally active ingredients, among them are the method comprising adding a corrigent such as a sweetener to a medicinally active ingredient and processing the mixture into a preparation, or the method in which the medicinally active ingredient is absorbed physically on a carrier" (see Office Action, pages 4-5, citing Col. 1, lines 20-31). However, upon a closer reading of the cited reference, these methods are discussed not because they are advantageous, but because those methods have many drawbacks (see Col. 1, lines 31-67). Therefore, Matoba '612 does not focus on these methods having drawbacks when disclosing its solid preparations comprising ion exchangers and active ingredients.

Thus, all three references of Matoba '612, JP '850, and Balkin '284, have been improperly combined. Any combination of these references only becomes obvious upon reading the Applicants' specification, and the improper application of hindsight (*i.e.*, JP '850 is discussed in the background section of Applicants' specification at page 1).

In view of the above remarks, Applicants respectfully submit that the present claims encompass subject matter that is patentably distinguishable from the cited references. Specifically, the present claims are patentable over the Matoba '612, JP '850, and Balkin '284

references. Accordingly, the Examiner is respectfully requested to withdraw all rejections and allow the currently pending claims.

Further, the Examiner is respectfully requested to enter this Reply After Final in that it raises no new issues. For example, new claims 22-27 add no new matter. Alternatively, the Examiner is respectfully requested to enter this Reply After Final in that it places the application in better form for Appeal.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Eugene T. Perez (Reg. No. 48,501) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Attached hereto is a marked-up version of the changes made to the application by this Amendment.

Pursuant to 37 C.F.R. § 1.17 and 1.136(a), Applicants respectfully petition a three (3) month extension of time for filing a response in connection with the present application. **The required fee of $920.00 has been submitted with the Notice of Appeal filed concurrently herewith.**

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment: Version with Markings to Show Changes Made

(Rev. 09/26/01)

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The paragraph beginning on page 7, line 20, has been amended as follows:

2 mg/ml of an aqueous donepezil hydrochloride solution was prepared. After 50 mg of κ-carrageenan, chondroitin sulfate or dextran sulfate was dissolved in 5 ml of the aqueous solution. Afterward, two examinees (which were represented by A and B in [Table)] Table 1) hold the whole amount of the solution in their mouths, and then evaluated the degree of a bitter taste and numbness in accordance with five grades. The results are shown in Table 1.

IN THE CLAIMS:

The claims have been amended as follows:

14. (Amended) The method according to claim 8 wherein the medicine is granules, fine granules, powders, liquids, syrups or jellies.

21. (Amended) The medicine composition according to claim 15 wherein the medicine is granules, fine granules, powders, liquids, syrups or jellies.

Claims 22-27 have been added.